

***Amendments to the Specification***

Please amend paragraph [0046] as follows:

[0046] Amino acid residues in HIV-1 Gag that are involved in the disruption of CA-SP1 processing by 3-*O*-(3',3'-dimethylsuccinyl) betulinic acid (DSB) were identified by sequencing the Gag-Pol gene of virus isolates that had been selected for resistance to DSB. The amino acid sequences from these resistant viruses were compared with the Gag-Pol gene sequences from DSB-sensitive HIV-1 isolates. Two single amino acid changes were identified in the DSB-resistant viruses, an alanine (Ala) to valine (Val) substitution at residue 364 (SEQ ID NO: 4) and in a second isolate, at residue 366 (SEQ ID NO: 6), in the Gag polyprotein (see Figure 4). These residues are located immediately downstream of the CA-SP1 cleavage site (at the N-terminus of SP1). Alanine is highly conserved at these positions throughout all HIV-1 clades in the Los Alamos National Laboratory database. The five amino acid residues upstream and downstream of the CA-SP1 cleavage site are also highly conserved among the various clades. However, isoleucine replaces valine ~~leucine~~ at the position two residues ~~one residue~~ upstream of the cleavage site in a number of clades (c.f., Figure 4, ~~SEQ ID NO: 1~~ SEQ ID NO: 1). (*"HIV Sequence Compendium 2002,"* Kuiken *et al.* eds. Los Alamos National Laboratory, Los Alamos, NM.)

Please amend paragraph [0053] as follows:

[0053] The present invention comprises a polynucleotide comprising a sequence which encodes an amino acid sequence containing a mutation in the HIV Gag p25 protein (CA-SP1), said mutation resulting in a decrease in the inhibition of processing of p25 (CA-SP1) to p24 (CA) by DSB. The polynucleotide of the invention includes a mutation which is optionally located near the CA-SP1 cleavage site or located in the SP1 region of CA-SP1. Said mutation can be present in an amino acid sequence that is selected from

the group consisting of KARVLVEAMS (SEQ ID NO: 2) or ~~KARVIAEVMS~~ KARILAEVMS (SEQ ID NO: 3). The polynucleotide of this invention is also drawn to sequences designated as SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8 or SEQ ID NO: 9. The invention also includes a vector comprising said polynucleotide, a host cell comprising said vector and a method of producing said polypeptides comprising incubating said host cell in a medium and recovering the polypeptide from the medium.

Please amend paragraphs [0074] and [0075] as follows:

[0074] The invention further includes a polypeptide containing a mutation in the CA-SP1 protein, said mutation which results in the decrease in inhibition of processing of p25 to p24 by 3-*O*-(3',3'-dimethylsuccinyl) betulinic acid, and also wherein said mutation is optionally located near the CA-SP1 cleavage site or located in the SP1 region of SEQ ID NO: 5 or SEQ ID NO: 7 (parental polynucleotide sequences) encoding the CA-SP1 protein. Said polypeptide may be encoded by a polynucleotide selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8 or SEQ ID NO: 9, or may comprise a sequence that is selected from the group consisting of KARVLVEAMS (SEQ ID NO: 2) or ~~KARVIAEVMS~~ KARILAEVMS (SEQ ID NO: 3). The polypeptide of this invention may further be encoded by a polynucleotide which hybridizes under highly stringent conditions to a polynucleotide selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8 or SEQ ID NO: 9. The invention also includes a polypeptide encoded by a polynucleotide which hybridizes to SEQ NO: 5, SEQ ID NO: 7 or SEQ ID NO: 10, which contains a mutation that results in decrease in inhibition of processing of p25 to p24 by 3-*O*-(3',3'-dimethylsuccinyl) betulinic acid, and also wherein

said mutation is optionally located in the SP1 region of CA-SP1. The polypeptide of this invention further includes polypeptides that are part of a chimeric or fusion protein. Said chimeric proteins may be derived from species which include, but are not limited to: primates, including simian and human; rodentia, including rat and mouse; feline; bovine; ovine; including goat and sheep; canine; or porcine. Fusion proteins may include synthetic peptide sequences, bifunctional antibodies, peptides linked with proteins from the above species, or with linker peptides. Polypeptides of the invention may be further linked with detectable labels; metal compounds; cofactors; chromatography separation tags, such as, but not limited to: histidine, protein A, or the like, or linkers; blood stabilization moieties such as, but not limited to: transferrin, or the like; therapeutic agents, and so forth.

[0075] The invention also includes an antibody which selectively binds an amino acid sequence containing a mutation in the CA-SP1 protein that results in a decrease in the inhibition of processing of p25 (CA-SP1) to p24 (CA) by 3-*O*-(3',3'-dimethylsuccinyl) betulinic acid and also wherein said mutation is optionally located in the SP1 region of CA-SP1. The invention also includes an antibody which selectively binds the polypeptide having a mutation which comprises a sequence that is one of KARVLVEAMS (SEQ ID NO: 2), ~~KARVLAEVMS~~ KARILAEVMS (SEQ ID NO: 3). Said antibody can selectively bind the polypeptide encoded by a polynucleotide sequence selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8 or SEQ ID NO: 9. Said antibody can also selectively bind the polypeptide encoded by a polynucleotide which hybridizes under highly stringent conditions to a polynucleotide selected from the group consisting of SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8 and

SEQ ID NO: 9. The invention also includes an antibody that is selectively binds to SP1, which would enable one to distinguish SP1 from CA-SP1. The invention also includes an antibody that selectively binds CA, which would enable one to distinguish CA from CA-SP1. The invention additionally includes an antibody that selectively binds at or near the CA-SP1 cleavage site. The antibody of this invention may be a polyclonal antibody, a monoclonal antibody or said antibody may be chimeric or bifunctional, or part of a fusion protein. The invention further includes a portion of any antibody of this invention, including single chain, light chain, heavy chain, CDR, F(ab')<sub>2</sub>, Fab, Fab', Fv, sFv, or dsFv, or any combinations thereof.

Please amend paragraphs [00121] and [00122] as follows:

[00121]        Pharmaceutical compositions of the present invention can comprise at least one of the compounds of Formula I or II disclosed herein. Pharmaceutical compositions according to the present invention can also further comprise other anti-viral agents such as, but not limited to, AZT (zidovudine, RETROVIR®, ~~Glaxo—Wellcome~~ GlaxoSmithKline), 3TC (lamivudine, EPIVIR®, GlaxoSmithKline), AZT+3TC, (COMBIVIR®, ~~Glaxo—Wellcome~~ GlaxoSmithKline), ddI (didanosine, VIDEX®, Bristol-Myers Squibb), ddC (zalcitabine, HIVID®, Hoffmann-La Roche), D4T (stavudine, ZERIT®, Bristol-Myers Squibb), abacavir (ZIAGEN®, ~~Glaxo—Wellcome~~ GlaxoSmithKline), nevirapine (VIRAMUNE®, Boehringer Ingelheim), delavirdine (~~Pharmacia and Upjohn~~ Pfizer), efavirenz (SUSTIVA®, DuPont Pharmaceuticals), saquinavir (INVIRASE®, FORTOVASE®, Hoffmann-LaRoche), ritonavir (NORVIR®, Abbott Laboratories), indinavir (CRIXIVAN®, Merck and Company), nelfinavir

(VIRACEPT®, ~~Agouron Pharmaceuticals~~ Pfizer), amprenavir (AGENERASE®, ~~Glaxo Wellcome~~ GlaxoSmithKline), adefovir (PREVEON®, HEPSERA®, Gilead Sciences), atazanavir (Bristol-Myers Squibb), and hydroxyurea (HYDREA®, Bristol-Meyers Squibb), or any other antiretroviral drugs or antibodies in combination with each other, or associated with a biologically based therapeutic, such as, for example, gp41-derived peptides enfuvirtide (FUZEON®, Roche and Trimeris) and T-1249, or soluble CD4, antibodies to CD4, and conjugates of CD4 or anti-CD4, or as additionally presented herein.

[00122] Additional suitable antiviral agents for optimal use with one of the compounds of Formula I or II of the present invention can include, but are not limited to, AL-721 (lipid mixture) manufactured by Ethigen Corporation and Matrix Research Laboratories; amphotericin B (FUNGIZONE®; Ampligen (mismatched RNA) developed by DuPont/HEM Research; anti-AIDS antibody (Nisshon Food); 1 AS-101 (heavy metal based immunostimulant); BETASERON® (β-interferon, Triton Biosciences); butylated hydroxytoluene; Carrosyn (polymannoacetate); Castanospermine; Contracan (stearic acid derivative); Creme Pharmatex (containing benzalkonium chloride) manufactured by Pharmalec; CS-87 (5-unsubstituted derivative of zidovudine); penciclovir (DENAVIR® Novartis); famciclovir (FAMVIR® Novartis); acyclovir (ZOVIRAX® ~~Glaxo-Wellcome~~ GlaxoSmithKline); HPMPC (cytofovir, VISTIDE® Gilead); DHPG, (ganciclovir, CYTOVENE®, Roche Pharmaceuticals); dextran sulfate; D-penicillamine (3-mercapto-D-valine) manufactured by Carter-Wallace and Degussa Pharmaceutical; FOSCARNET® (trisodium phosphonoformate; Astra AB); fusidic acid manufactured by Leo Lovens; glycyrrhizin (a constituent of licorice root); HPA-23 (ammonium-21-

tungsto-9-antimonate; Rhone-Poulenc Sante); human immune virus antiviral developed by Porton Products International; ORNIDYL® (eflornithine; Merrell-Dow); nonoxynol; pentamidine isethionate (PENTAM-300) manufactured by Lypho Med; Peptide T (octapeptide sequence) manufactured by Peninsula Laboratories; Phenytoin (~~Warner-Lambert~~ Pfizer); INH or isoniazid; ribavirin (RIFADIN®, Aventis); (VIRAZOLE®, ~~ICN~~ Valeant Pharmaceuticals); rifabutin, ansamycin (MYCOBUTIN® Pfizer); CD4-IgG2 (Progenics Pharmaceuticals) or other CD4-containing or CD4-based molecules; Trimetrexate manufactured by ~~Warner-Lambert~~ Pfizer; SK-818 (germanium-derived antiviral) manufactured by Sanwa Kagaku; suramin and analogues thereof manufactured by Miles Pharmaceuticals; UA001 manufactured by Ueno Fine Chemicals Industry; and WELLFERON® ( $\alpha$ -interferon, ~~Glaxo-Wellcome~~ GlaxoSmithKline).

After the abstract, and before the drawings, please add the sequence listing attached hereto.